Prediction of inhaled drug targeting based on in vitro assessment of nebulizers and aerosol deposition modeling

Tomasz R. Sosnowski, Izabela Kazimierczak, Aleksandra Sawczuk
Faculty of Chemical and Process Engineering, Warsaw University of Technology, Poland

We proposed a new method for the quantitative assessment of the targeted delivery of inhaled drugs administered from nebulizers, using the principles of mass balance for such drug delivery devices. The deposited mass fluxes in different parts of the respiratory system were evaluated based on (1) the experimental results of nebulizer performance (including the rate of drug release and particle size distribution represented by the mass median aerodynamic diameter, MMAD, and geometric standards deviation, GSD), and (2) calculations of regional deposition of inhaled therapeutic aerosol using the Multiple Path Particle Dosimetry (MPPD) model [1]. The application of proposed approach was demonstrated based on the results of a case study done for selected vibrating mesh nebulizers (VMN), including a possibility of using a valved holding chamber (VHC) as an add-on device to increase the pulmonary availability of the drug-containing aerosol [2].
It was assumed that for the best clinical effect, the sum of deposited mass fluxes ($\dot{m}$) of a drug in the trachea-bronchial (TB) and pulmonary (P) regions should prevail the flux of drug deposited in the upper airways (H) which can lead to side effects of inhalation therapy (in particular, for glucocorticosteroids). Therefore, the parameter of the "Therapeutic Index", TI, was defined as:

$$TI = \dot{m}_P + \dot{m}_{TB} - \dot{m}_H \quad (1).$$

Table 1 shows the results of experiments and calculations done for a single drug (budesonide) nebulized in a selected VMN working alone or with the attached VHC. They show that adding VHC results in a nearly twofold increase in aerosol emission rate (which agrees with the published data [2]) but, at the same time, to a decrease in MMAD and GSD (i.e., a narrowing of the size distribution). As a result, the TI value has doubled, confirming that the use of VHC with this nebulizer significantly increases targeting of tested medicine to the lower respiratory tract.
Proposed approach provides a methodology for the quantitative assessment of the expected clinical effects of nebulizers and inhalers used with different drugs and various configurations.

Table 1. Experimental and calculated data for the tested VMN, VHC, and a selected drug.

Configuration of nebulization system	Experimental results			Calculated results (MPPD)			
	Aerosol emission rate [g/min]	MMAD [μm]	GSD [-]	Regional deposition efficiencies in the respiratory system			TI
				H	TB	P	
VMN alone	0.087	3.44	1.71	0.548	0.178	0.265	0.029
VMN+VHC	0.165	3.10	1.66	0.514	0.163	0.271	0.058

References:

1. Multiple-Path Particle Dosimetry Model (MPPD) v. 3.04. 2016. Applied Research Associates, Inc. (ARA), Albuquerque, NM, USA.
2. Sosnowski T.R., Kazimierczak I., Sawczuk A., Janeczek K., Emeryk A. 2025. Improving pulmonary delivery of budesonide suspensions nebulized with constant-output vibrating mesh nebulizers by using valved holding chamber. Pharmaceutics 17, 696